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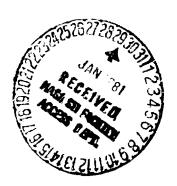
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# LOCAL REDISTRIBUTION OF BLOOD UNDER THE EFFECT OF FIXATION STRESS AGAINST A BACKGROUND OF HYPOKINESIA

O.A. Kovalev, V.F. Lysak, V.I. Severovostokova, S.K. Sheremetevskaya

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NATIONAL AERONAUTICS AND SPACE ADMINISTRATION WASHINGTON, D.C. 20546 AUGUST 1980

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## LOCAL REDISTRIBUTION OF BLOOD UNDER THE EFFECT OF FIXATION STRESS AGAINST A BACKGROUND OF HYPOKINESIA

O.A. Kovalev, V.F. Lysak, V.I. Severovostokova, S.K. Sheremetevskaya<sup>1</sup>

Fixation stress may be considered an experimental model of emotional disturbance. Immobilization of rats on a stand is associated with pronounced shifts in local blood distribution [4]. However, the effect of previous restrictions on mobility on local redistributions of blood which result from fixation stress has not been studied.

#### The Method of Investigation

Experiments were conducted on mongrel male rats of mass 190-230 g. Hypokinesia was created by placing the animals in the usual body position in a narrow cage made from organic glass. While the rats were kept in the cage, their random movement was substantially restricted in all directions. The duration of the exposure was 7 days (HK-7). The rats were kept on normal laboratory rations. Food was removed from the feeder for the final 18-20 hours preceding the experiment but water was kept in the fountain.

fixation stress resulted from attaching the animals to the lathe on their backs for periods from 1 to 4 hours. Immediately after tying

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<sup>1</sup> Central scientific-research laboratory of the Doctors' Training Institute. Faculty of Pathological Physiology of the Leningrad Military Medical Academy

<sup>\*</sup> Numbers in the margin indicate pagination in the foreign text.

a catheter was introduced into the external jugular vein using a local anesthetic, an 0.5% solution of novocaine. In the control group (HK-7 without fixation on the stand) the catheter was inserted 2-3 days before the experiment. Fourteen rats were used in each of the basic and the control series.

In order to study disturbances in carbohydrate exchange which result from prolonged hypokinesis [5], we studied several indices of carbohydrate exchange. The concentration of lactic (IA) and pyroracemic acid in the blood and their ratio (IA/PRA) and the surplus of lactate (SL) were determined by generally accepted methods [9, 10]. These indices were studied in three additional series of experiments (control HK-7, fixation for 1 and 4 hours against a HK-7 background), each of which involved 12 rats. In studying the systemic hymodynamic indices we measured pressure in the main carotid artery (AP) by a direct method involving a mercury menometer, the number of heart contractions (MHC), by electrocardiogram taken in the And Standard Land, the volume of circulating blood (VCB), by culturing erychrocyte-chromium-51 and albumin-iodine-131.

In order to record local redistributions of blood, erythrocytes from a rat donor which were marked by chromium-51 isotope, and albumin from human serum marked by iodine-131 were introduced internally. The ratio of the radioactivity of the marked erythrocytes to the total activity of the mixture introduced to the rat equalled the individual hematocrite of the blood, found from a tail section. The total volume of the indicator mixture was 0.1 ml, its total radioactivity, approxi-

mately 10 micross. After even mixing in a vascular alveus, the time of which was established experimentally for the prescribed element indicator to be 10 minutes, for the plasma indicator 3 minutes, the internal introduction of 0.7 ml saturated potassium chloride solution caused cessation of heart activity. The corpse was frozen at -20° C in for 2 hours. The organs and tissues listed in Table 2 were removed by dissection. The radioactivity of the sample was proportional to the amount of blood. We analyzed only the change in the experiment in relation to the control. The method has been described previously and substantiated. In particular, we obtained proof of the fact that changes observed in local blood distribution by this method occur during life, despite the fact that we used heart stoppage [1].

In analyzing the results, apart from evaluating the probability of differences appearing in the arithmetic means following Student's first criterion, we used factor analysis in a modification which enables us to find the multidimensional nature of changes from the control to the experiment [3]. Quantitative processing was done on electronic computer M-222.

### Results of the Investigations and Discussion

Changes in the systemic hemodynamics indices and carbohydrate exchange indices during fixation stress against a background of hypokinesia are characterized by the data presented in Table 1. The results obtained allow us to note moderate hypotension during immobilization for 4 hours along with an increase in LA in the blood and in the LA/

TABLE 1
SOME INDICES OF SYSTEMIC MEMODYNAMICS AND CARBOHYDRATE EXCHANGE
IN RATS DURING FIXATION STRESS (IMMOBILIZATION ON A STAND)
AGAINST A BACKGROUND OF SEVEN-DAY HYPOKIMESIA (HK-7)

|  | Control<br>(au 12)   | Immobilization on a lathe, |                     |                   |                  |                |
|--|--|----------------------------|---------------------|-------------------|------------------|----------------|
| Investigated indices   | (MX+Z)<br>(MXm/)   | RCa                        | P <sub>1-2</sub>    |                   | P <sub>1-3</sub> |                |
| Pressure in the main earetid artery (AP), am mercury               |  |                            | 50                  | t to              | <0.02            | > '            |
| Number of heart contractions (NMC) per 1 minute                    | es de la companya de | age of the                 | >1                  | 29 M.             | >0.              | Z0 05          |
| Amount of circulating blood (VCB), mg blood per I g mass           | * * •  |                            |                     | 7 <b>4</b> - 1704 | ×                | >              |
| Lactic acid (IA) concentra-<br>tion in blood, mmole/1              |  |                            | < 0.05 € 0.05       | 1.1               | <0.03            | ·              |
| Pyroracemic acid (PRA) con-<br>centration in the blood,<br>mmole/1 |  | 21300                      |                     |                   |                  |                |
| Ratio of LA/PRA  |  | · ; · · , .                | ε <sub>ε</sub> θ θ5 | j.                | 0.001            | ₹0-05          |
| Surplus of lactic acid (lactate surplus-SL), mole/1                |  |                            | ~0.001 .            |                   | <0.001 ·         | <0.00 <b>1</b> |

PRA and SL. The shifts in the indices of carbohydrate exchange were more pronounced during 4 hours of fixation stress. The NHC, VCB and the PRA concentration in the blood did not change substantially. Evidently, the data obtained indicate clear signs of metabolic disturbances with insignificant changes in systemic hemodynamics.

An evaluation of relative changes in local blood distribution is presented in Table 2. In the "control" flow sheet we show arithmetic means (M) and the mean standard deviation (\*m) of the percent of the volume of circulating blood (% VCB) for a given vascular re-

gion in rats subjected to seven day hypokinesia (HK-7) without fixation stress. In the "p" and "f<sub>1</sub>" flow sheets we show probable evaluation of changes in comparison with the control, relative to Student's t-criterion and to factor I loads. The sign "+" after the value "p" and the sign "+" of the factor load designate an increase in the relative concentration of blood, the sign "-" designates a decrease. Loading factor I (f<sub>1</sub>) quantitatively characterises the interrelation, relative to this factor, in the organ or tissue with shifts in all the other investigated vascular regions. Factor loading is statistically significant (p 0.05) with an absolute -- are greater than or equal to 0.360. The weight of factor I substantially exceeded the weight of II and subsequent factors; this indicates its decisive contribution to the integral evaluation of changes from the control to the experiment.

The results presented in Table 2 show that fixation stress causes a redistribution of circulating blood from the liver and several internal organs in the animal to the lungs, skin and especially the muscular and bone tissue in various parts of the body. During one hour fixation /123 stress, a n-criterion evaluation indicated an increase in blood in the adrenal glands. Evidently, the basic direction of local redistributions of blood is determined by a decrease in its concentration in the largest of the investigated sections of the blood channel, the liver. Changes were basically of a similar character during immobilization on a significant a HK-7 background for 1 and 4 hours.

The local redistributions of blood described differ significantly from observations made during fixation stress in rats which were not

TABLE 2
THE CHANGE IN THE RELATIVE BLOOD CONCENTRATION (% VCB) IN ORGANS AND TISSUES IN RATS DURING FIXATION STRESS (INMOBILIZATION ON A STAND ) AGAINST A BACKGROUND OF SEVEN-DAY HYPOKINESIA (HK-7).

| Tissues and organs                                     | Control<br>(HK-7)<br>M-m | Eval             | Evaluation of changes durin impobilization for 1 hr 4 hr |              |                             |  |
|--|--------------------------|------------------|--|--------------|-----------------------------|--|
|  |                          | P                | fı   | p            | f                           |  |
| Head:<br>Skin  |                          | • .              |  |              |                             |  |
| Muscles and bones<br>Brain                             | ÷                        |                  | 1 3 19<br>1 3 19   |              | - 0 ,429<br>- 0 ,411<br>- 2 |  |
| Meck:<br>Skin<br>Muscles and bones                     | . 1                      | );<br>};         |  | <del>}</del> |                             |  |
| <u>Chest</u> :<br>Skin                                 |                          | * .              |  |              |                             |  |
| Muscles and bones<br>Myocardium<br>Lungs               |                          |                  | t w.   |              | .254<br>6.754<br>           |  |
| Abdomen:<br>Skin                                       |                          |                  |  |              |                             |  |
| Muscles and bones<br>Liver<br>Small intestine          |                          |                  | er e                 | > 1          | 0.1601<br>0.1801            |  |
| Large intestine<br>Stomach<br>Kidneys<br>Adrenal gland |                          | >                | 1 . <b></b>  |              | 0.511<br>- 0.405            |  |
| Spleen<br>Pencreas                                     |                          | -20 05<br>-20 05 | (F. 60)  | 0 (c) (d)    | 0,602                       |  |
| Urinary bladder<br>Testicles                           |                          |                  |  |              |                             |  |
| Front extremities:<br>Skin                             |                          | ٠,               | -  |              |                             |  |
| Muscles and bones  Back extremities:                   | •                        | 200              | <i>0</i> 407   | KJO UM       |                             |  |
| Skin<br>Muscles and bones                              |                          |                  |  |              |                             |  |
| Teil .   |                          |                  |  |              |                             |  |
| Total:<br>Skin<br>Muscles and bones                    |                          |                  |  |              |                             |  |

TABLE 2

| Tissues and organs  | Control<br>(HK-7)<br>M <u>+</u> m | Evaluation of changes during impobilization for 1 hr 4 hr |                |   |                         |
|---|-----------------------------------|---|----------------|---|-------------------------|
|   |                                   | р_  | f_             | P | f1                      |
| Internal organs Weight of factor 1, % Weight of factor 2, % |                                   |   | 4.881<br>27,40 | > | - 0.386<br>2 .9<br>14.8 |

subjected to preliminary hypokinesia. Thus, during immobilization of the intact animals on the chang on their backs for I hour, the relative concentration of blood decreased in many of their internal organs (stomach, pancreas, small and large intestines, spleen, urinary bladder, testicles), but it did not change in the liver. Blood concentration was also reduced in the muscular and bony tissues of the extremities, to a lesser extent in the muscles of the abdomen and small coxa and in the skin of the back extremities and the chest. The percent concentration of blood increased in the brain, the myocardium, the lungs, the muscular and bony tissues of the head, the neck and the chest. The fixation of intact rats on a street back down, for 4 hours was associated with a decrease in blood concentration in the skin, the muscular and bony tissues (with the exception of the vascular regions of the head and neck, where changes were insignificant), the internal organs, the stomach, the pancreas, the small and large intestines, the spleen, the urinary bladder and the testicles. The blood concentration increased in the liver, the myocardium and the lungs [4].

We may assume that fixation stress in intact animals is associated with a disturbance in the sympathetic nervous system (SNS) and the hypothalamus hypophysis adrenal system (HHAS) which results from an in-

crease in vascular tonus. In this case, fixation for I hour is characterized by more pronounced structural effects on the capacity and resistive vessels of organs in the "splanchnic" region, the skeletal muscles of the extremities, the abdomenaaridaths small coxe, the skin of the back extremities and the skin of the chest, as a result of which there is a redistribution of blood. Results of investigations with a quantitative comparison of neurohumoral structural vascular effects [6, 3] indicate the validity of this explanation. Fixation on the time. for 4 hours evidently strongthens the neurohumoral vascular constricting effect in comparison with immobilization for 1 hour, which results in a general considerable constriction of capacity vessels as the previous shift in the local tonus of the resistive vessels is maintained. The absence of changes in the blood concentration in the vascular regions of the head and neck and the increase in blood concentration in the liver, myocardium and lungs tend precisely to this explanation. Evidently, the flow of blood through the portal vein system during fixation stress in intact animals is decreased because of the constriction of the vessels in organs in the splanchnic region. Under these conditions, not only the increase in blood concentration in the liver during 4 hour fixation, but also the absence of changes during I hour fixation must be considered as a reflection of the arterialization of liver blood concentration.

Prolonged hypokinesia by itself is characterized by clear symptoms of SNS and HHAS disturbance [7, 11]. For this reason, the additional effect on the organism of fixation stress against a HK-7 background may cause exhaustion of neurohumoral constriction effects as well as local vascular expanding effects resulting from metabolic dis-

turbances, the reflection of which may be the changes in the indices of carbohydrate exchange which we have studied. Other circumstances support this explanation. In the first place, specifically in the skeletal muscles, shifts in the functional activity of which are fundamental during hypokinesia, the increase in the quantity of blood is very pronounced. In the second place, a relative reduction in the blood concentration is not specific to fixation stress against a background of hypokinesia. It is also observed in other effects on the organism which are accompanied by symptoms of metabolic disturbances, which may exert local vescular constricting effects on the skin, skeletal muscles and several internal organs [2].

A detailed explanation of the mechanisms of the effect of preceding /12/
hypokinesia on the local redistribution of blood, which results from
fixation stress, requires further investigations.

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